DECLARE – TIMI 58
Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events

Discussant

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Please specifically note RWI relevant to the management of diabetes Astra Zeneca, Boehringer Ingelheim, Janssen, Sanofi, Novo Nordisk and Merck
Type 2 Diabetes Mellitus - Facts

- High-risk for mortality
- CV mortality - number 1 cause of death
- Risk for “macrovascular” complications
  - MI, PVD, and Stroke
- Risk for “microvascular” complications
  - Retinopathy, Neuropathy, and Nephropathy
- Risk for heart failure
- Worse outcomes with these complications
- PREVENTION and TREATMENT of these complications central to T2DM management
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• Well conducted trial
• Highest proportion of patients with risk factor but without established ASCVD among SGLT2i trials
• Confirms and replicate data from other studies with SGLT2i
  – Safety
  – HbA1c
  – Blood pressure
  – Weight
SGLT2i and T2DM

Pump, pipes, and filter: do SGLT2 inhibitors cover it all?

Subodh Verma et al. Lancet 2018
Interpretation

• SGLT2i data cannot be taken in isolation from other T2DM trials and therapies
• All CV complications are all important
• Microvascular and macrovascular designation
  – Biologically overlapping
  – Not distinct concepts
• Macrovascular does not include heart failure
• CKD in T2DM should be studied independent of other “microvascular” diseases
Heart Failure and T2DM

If 5 RF were controlled (HgA1c, smoking, LDLc, BP, albuminurinia)

HR for AMI–0.84 (0.75-0.93)
HR for stroke–0.95 (0.84-1.07)

HR for HF – 1.45 (1.34-1.57)
Treatment - T2DM

• Differentiation between ‘micro’ and ‘macro’ vascular disease has limited clinical utility
• ‘Primary’ and ‘secondary’ prevention cohort for one disease may or may not have relevance to another disease
• For patients similar to those studied in the trials – SGLT2i should be used for incident HF risk reduction, irrespective of their effect on MACE outcomes
• For patients not studied adequately e.g. T2DM with no clear risk factors or with manifest HF – further data are needed